CASE STUDY

Health Decisions

Diagnostics Health

510(k) Study of Respiratory Diagnostic

Test Diagnostic: A multiplexed nucleic acid test intended for use with instrument X for the qualitative *in vitro* detection and identification of multiple respiratory viral pathogen nucleic acids in nasopharyngeal swabs (NPS) obtained from individuals with suspected respiratory tract infections.

Comparator product for substantial equivalence determination: Culture/Direct Fluorescent Antibody (DFA) with viral subtype confirmed by RT-PCR/bidirectional sequencing as indicated. Viruses without a DFA test were identified by two independent PCR reactions and bidirectional sequencing.

Patient Population: Subjects exhibiting one or more symptoms/signs suggestive of respiratory infection and having fever within 5 days of study visit, not having received an intranasal influenza vaccine, influenza antiviral medication or an investigational drug treatment currently or within the previous 30 days of study enrollment, with no contraindication for nasopharyngeal swab.

Study Design: Collect samples and compare investigational assay to the established gold standard reference method of viral culture for most viral targets. For respiratory viruses in which culture was not available, a composite (multi-test) reference method (a predetermined algorithm that combined the results of multiple tests) was used as the comparator method.

Challenges Faced:

- Collecting samples rapidly during a flu season of approximately 3 months despite condensed startup timelines
- Ensuring effective sample tracking to prevent loss of any samples
- Ensuring sample integrity through proper sample collection and shipment
- Ensuring effective cohort management to meet goals for demographic diversity

Study at a Glance

Type of Study:

510(k)

Objective:

Obtain data to support 510(k) submission

Active Sites:

3 CLIA-certified (high-moderate complexity) laboratories in the U.S. with geographic diversity

Subjects Enrolled:

1171

Evaluable Samples:

1048

Risk Management and Mitigation:

The following strategies for risk management and mitigation were among those that Health Decisions utilized in this study.

Ensuring Rapid Collection of Samples during Flu Season – The sponsor had to conclude discussions with regulators and complete a variety of logistical arrangements and was left with an unusually brief period between study startup and the target period for sample collection – fall flu season. In addition, there is always the risk that a chance season of low incidence of respiratory infections will cause sample collection to lag behind projections. Health Decisions managed site selection and startup effectively to ensure activation of all sites before flu season commenced. Health Decisions selected diverse sites with a strong track record in similar diagnostics studies, provided detailed training in subject recruitment and consenting and strong encouragement to focus on identifying and enrolling eligible subjects as rapidly as possible. Health Decisions tracked enrollment closely to ensure satisfactory progress toward enrollment goals. Sites that lagged behind enrollment targets received followup calls and re-training as necessary.

Ensuring Effective Sample Tracking – With seasonal illnesses such as respiratory infections, it is difficult to replace any missing samples collected in the fall by collecting new samples in spring, when incidence is low. Therefore, Health Decisions used a proprietary barcode-based sample-tracking system to ensure effective tracking of every sample collected. The tracking system required entries when each sample was collected, received at a laboratory, placed into frozen storage and shipped to the sponsor. Health Decisions was able to follow each sample through this cycle and no samples were lost.

Ensuring Sample Integrity – Sample-collection procedures were highly specific. For example, if nasopharyngeal swab samples were collected as standard of care from one nostril, the study sample was to be collected from the other. Study requirements included refrigeration of samples at 2-8°C at sites and -70°C following testing. For the comparator, viral cultures had to be inoculated within 12 hours. Health Decisions ensured sample integrity through a variety of proactive measures, including detailed instructions for sample collection in the study manual, a training video and webex training. In addition, if there were deviations in collection procedures at a site, Health Decisions provided timely follow-up and re-training. Sample tracking information was important in confirming sample shipment from sites and receipt by laboratories within the time window specified in the protocol.

Ensuring Effective Management of Demographic Cohorts – Although requirements for demographic diversity were relatively modest because this type of respiratory virus diagnostic has a broad intended-use population, it was essential to ensure diversity in the subject population that accurately reflected the intended-use population in terms of gender and age. Therefore, samples were collected at a variety of sites as described above. Health Decisions monitored demographics from CRF data throughout the study to ensure desired representation of each cohort. The study met all goals for demographic diversity. For example, of the 1037 evaluable samples, approximately half were from male subjects and half from female patients, approximately one quarter of the samples were collected from children under the age of 1 and the majority of samples were collected from patients ages 21-65.